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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/188,051	11/06/1998	BRET A. SHIRLEY	5784-25	3829

7590 12/31/2002

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	32

DATE MAILED: 12/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/188,051	SHIRLEY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-48 and 85-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-48 and 85-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. The finality of previous Office Action (Paper No. 25) is withdrawn because a new ground of rejection is applied in this Office Action.

Status of the Claims

2. Claims 29-48 and 85-112 are pending.

Applicants' supplemental amendment filed on December 2, 2002 (Paper No. 31) has been entered, and applicants' response has been fully considered. Claims 29, 31, 46, 85, 99 and 101 have been amended. Thus, claims 29-48 and 85-112 are examined.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because it indicates the instant application claims the benefit of U.S. Provisional Application No. 60/064,891, filed November 7, 1997 under 35 U.S.C. §120, the priority should be claimed under 35 U.S.C. § 119(e).

Rejection Withdrawn

Claim Rejections - 35 USC § 112

4. The previous rejection of claims 29-48 and 85-112 under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' amendment to the claims, and applicants' response at pages 3-5 in Paper No. 31.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 29-40, 44-48, 85-93, 97-107, 111 and 112 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 10-14, 16, 17, 18 and 20 of copending Application No. 09/187,661.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 29-40, 44-48, 85-93, 97-107, 111 and 112 in the instant application disclose a composition having a pH of 5.5 or greater, comprising IGF-I or a biologically active analog thereof having an amino acid sequence which shares at least 70% sequence identity to human IGF-I at a concentration of 12 mg/ml or greater, and at a temperature of about 4 °C, and a solubilizing compound comprising a guanidinium group, wherein the solubilizing compound is in an amount sufficient to make IGF-I or analog thereof soluble at a concentration of 12 mg/ml or greater, and at a temperature of about 4 °C. This is obvious in view of claims 1, 2, 5, 10-14, 16, 17, 18 and 20 in the copending application which disclose a low salt-containing aqueous composition comprising human IGF-I or a biologically variant thereof in a concentration of at least 250 mg/ml and a pH greater than about 5.0, wherein the variant is a polypeptide which has at least 80% sequence identity to human IGF-I. Since the low salt-containing composition can be a composition containing a salt such as arginine, guanidine·HCl or other arginine compounds in an amount that makes IGF-1 or its analog more soluble at higher concentration and at about 4

°C, thus, both sets of claims encompass a low salt-containing (e.g., arginine) aqueous composition comprising human IGF-I or a biologically variant thereof at a concentration of at least 250 mg/ml and a pH greater than about 5.5, wherein the variant is a polypeptide which has at least 80% sequence identity to human IGF-I. Thus, claims 29-40, 44-48, 85-93, 97-107, 111 and 112 in present application and claims 1, 2, 5, 10-14, 16, 17, 18 and 20 in the copending application are obvious variations of a low salt-containing (e.g., arginine) aqueous composition comprising human IGF-I or a biologically variant thereof at a concentration of at least 250 mg/ml and a pH greater than about 5.5, wherein the amount of arginine compound that makes IGF-I or its analog more soluble at about 4 °C.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 29-44, 46-48, 85-97 and 99-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Florin-Robertsson *et al.* (WO 94/15584) taken with Ron *et al.* (U.S. Patent 5,597,897).

Florin-Robertsson *et al.* (WO 94/15584) teach an IGF-I formulation containing human recombinant IGF-I or a functional analog thereof (claims 33, 34, 47) in 5-50 mM phosphate buffer, where the pH of solution is 5.5-6.5, preferably 5.7-6.2 (claims 38-40, 91-93, 105-107) and the solution is isotonic, which is made of NaCl (e.g., Examples, 6.43 mg/ml or 8.48 mg/ml, corresponding to 110 mM or 130 mM; about 150 mM, claims 44, 48, 97, 100, 111), the concentration of IGF-I is dependent of its solubility in the used buffer, preferably the concentration of IGF-I is 1-100 mg/ml, more preferably 1-20 mg/ml at 5 or 25 °C (page 6, line 22-page 7; page 21, line 21; Examples; claims 41-43, 94-96, 108-110). However, Florin-Robertsson *et al.* do not teach the use of a solubilizing compound comprising a guanidinium group in the formulation. Ron *et al.* teach an effective amount of a solubilizing compound such as arginine and guanidine (e.g., 50-600 mM of arginine, preferably 300-500 mM; column 2, lines 34-42; column 3, lines 26-28; claims 30-32, 35-37, 86-90, 102-104) is used for preparing a pharmaceutical formulation containing osteogenic protein. At the time of invention was made, it would have been obvious to one of ordinary skill in the art to include a solubilizing compound taught by Ron *et al.* to prepare an IGF-I formulation as taught by Florin-Robertsson *et al.* having a stabilized IGF-I solution at the higher concentration (e.g., >12 mg/ml) and at higher pH (e.g., > pH 5.5) for therapeutic use (claims 29, 46, 85, 99, 101). Thus, the combined references result in

the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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December 27, 2002

Christopher S. F. Low
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